

REMARKS

Amendments to the Specification

The specification has been amended to delete reference to Figure 10C. Figure 10C is not necessary for the understanding of the subject matter sought to be patented. Deletion of Figure Legend 10C is required to make the Figure Legends consistent with the Figures submitted with the application. No new subject matter is introduced by this amendment.

Amendments to the Claims

Claim 1 has been amended to include the recitation that the oligonucleotide has one or more phosphorothioate internucleoside linkage(s). Support for this amendment can be found throughout the Specification and in Claim 5 as originally filed. No new matter has been added.

Rejection of Claim 1 Under 35 U.S.C. §102(b) or §103(a)

Claim 1 is rejected under 35 U.S.C. §102(b) or §103(a) as being anticipated by or obvious over Accession Number AA469268 from NCI-CGAP (National Cancer Institute, Cancer Genome Anatomy Project).

Claim 1, as amended herein, recites an oligonucleotide having a nucleotide sequence of from 15 to about 26 nucleotides and having one or more phosphorothioate internucleoside linkage, that inhibits one or more specific histone deacetylase isoforms, but less than all histone deacetylase isoforms, wherein the oligonucleotide is complementary to a region of RNA or double-stranded DNA that encodes a portion of HDAC-1 (SEQ ID NO: 2). Accession Number AA469268 neither teaches nor suggests an oligonucleotide having one or more phosphorothioate internucleoside linkage(s). Thus Claim 1, as amended, is neither anticipated nor made obvious by Accession Number AA469268. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-3 and 5 Under 35 U.S.C. §103(a)

Claims 1-3 and 5 are rejected as being unpatentable over Yoshida *et al.*, (hereinafter "Yoshida"), in view of the collection of Taylor *et al.*, (DDT vol. 4, No. 12, 12/12/99, pages 562-567), Bennett *et al.*, (Chapter 2, pages 13-46, from Methods in Molecular Medicine: Antisense

Therapeutics, 1996), Baracchini *et al.*, (U.S. Patent 5,801,154), Cowser (U.S. Patent 5,951,455) and the sequence of HDAC-1 (GenBank Accession No. U50079).

As previously argued, the combination of Yoshida and others fails to render the claimed invention obvious because there is no motivation or suggestion, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. According to the Examiner, the motivation to combine Yoshida with the other references is that Yoshida taught the need for “the use of a **more specific and potent inhibitor** of histone deacetylase... to carry out further more refined analysis” (emphasis added). However, the Examiner continues to take this statement out of context.

Yoshida describes that prior to their publication n-butyrate, a small molecule inhibitor of histone deacetylase, was used with pleiotropic effects on other enzymes, cytoskeleton, cell membranes, etc. Thus, the technical problem faced by Yoshida was to find a more specific and potent small molecule inhibitor of histone deacetylase than n-butyrate. Yoshida solved this problem by using another small molecule inhibitor of histone deacetylase referred to as (R)-Trichostatin A (hereinafter “TSA”).

Yet the Examiner maintains that Yoshida not only provides the motivation to find further “more specific and potent inhibitors” of histone deacetylase but also provides the motivation to look outside the small molecule inhibitor art to antisense technology even though (a) TSA is the more specific and potent inhibitor Yoshida describes a need for and (b) there is no mention, explicitly or implicitly, within Yoshida that antisense technology could be used to provide specific and potent inhibitors of histone deacetylase. Yoshida described a technical problem and its solution and fails to provide motivation to do anything but use TSA as a histone deacetylase small molecule inhibitor.

Accordingly, Applicants respectfully reiterate that there is no motivation in the prior art to combine the cited references. Thus, Applicants respectfully request that the rejection of Claims 1-3 and 5 for obviousness be withdrawn.

Allowable Claim(s)

Applicants acknowledge that the Examiner found Claim 7 to be free of prior art.

Notice of Appeal

A Notice of Appeal for twice rejected Claims 1-3 and 5 is being filed concurrently herewith.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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